herewith acknowledged with appreciation. For reasons as urged at said interview set forth and further elaborated upon below, the Examiner agreed that limiting the claims to the method of making, i.e., to the method to which the claims have now been limited, would potentially place the case in condition for allowance. Such has been done, the application being limited to claims directed to the method of making.

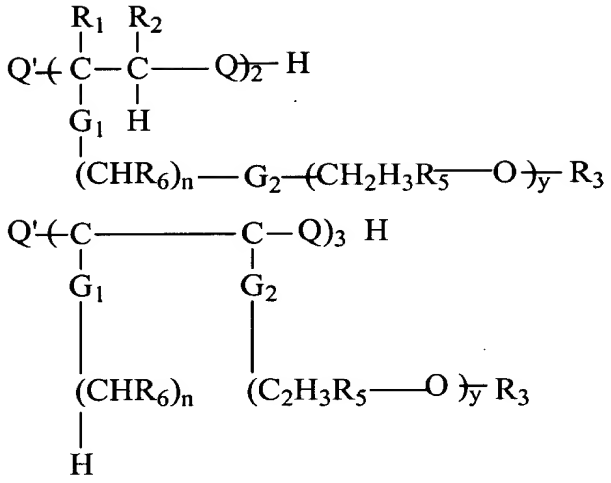
Specifically, the claimed invention has now been restricted to a method for preparing a drug targeting system for administering one or more physiologically effective substances to a mammal, said method comprising:

a) preparing nanoparticles made of a polymeric material, said nanoparticles being free of a surfactant surface coating and comprising said polymeric material, one or more physiologically effective substances to be delivered to said mammal, and one or more stabilizers for said nanoparticles allowing targeting of said one or more physiologically effective substances to a specific site within or on a mammalian body, said one or more stabilizers being selected from the group consisting of polysorbate 85, polysorbate 81, dextran 12,000, carboxylic acid esters of glycerol, sorbitan monostearate, sorbitan monooleate, polyoxamer 188, polyoxarnines, alkoxylated ethers, alkoxylated esters, alkoxylated mono-, di and triglycerides, alkoxylated phenols and diphenols, Genapol® compounds, Bauki compounds®, sodium stearate, metal salts of alcohol sulfates and metal salts of sulfosuccinates and mixtures of two or more of said substances, wherein said Genapol® compounds are of the formula

$CH_3(CH_2)_y$ - $(O\text{-}CH_2\text{-}CH_2)_x$-OH

wherein y is in the range of 4 to 18 and x is in the range of 1 to 18,

and said Bauki® compounds are of the formulas (I) or (I')



(I)

(I')

in which R_1, R_2, R_5 and R_6 are identical or different and represent hydrogen and a methyl or ethyl group,

Q represents a valency, oxygen or an ester or amide bridge and Q' denotes hydrogen if Q represents a valency or oxygen, and is a hydroxyl or amino group if Q represents an ester or amide bridge,

x is an integer from 3 to 50, if Q is a valency or oxygen, and an integer from 3 to 1000, if Q is an ester or amide function, G_1 and G_2 are a valency, oxygen or an ester or amide group, it being possible for the two groups to be identical or different, n is an integer from 4 to 44,

y is an integer from 2 to 50, and R_3 is hydrogen or a lower alkyl having 1-6 C atoms, and; by polymerizing one or more monomeric or oligomeric precursors of said polymeric material or both, in the presence of said one or more physiologically effective substances and in the presence of said stabilizers; and optionally

b) providing said nanoparticles in a medium allowing the transport of said nanoparticles to a target within or on said mammal after administration.

A significant feature neither disclosed nor made obvious by the references is the

limitation "polymerizing one or more monomeric or oligomeric precursors of said polymeric material or both, in the presence of said one or more physiologically effective substance and in the presence of said stabilizer". Such is not the case in the cited references. In neither Canal nor Bernstein, the primary references, are the monomers of the polymeric material polymerized in the presence of the one or more physiologically effective substances and in the presence of a stabilizer. Rather, in the prior art the surfactants and stabilizers are added subsequently to the polymeric material to modify the interface properties of the particles. Only coating of the particles is disclosed by the prior art, this also being contrary to the express requirements of the claims of "being free of a surfactant surface coating" and being prepared by the claimed means resulting in a significantly and materially different composition. Note, in particular, page 4, lines 25-27 of Canal, this reference is clearly teaching away from the claimed invention. Similarly, in Bernstein, already polymerized particles are employed. The Examiner at said interview thus agreed that the method of making claims, to which they are now limited, would potentially appear to be allowable.

The subsidiary references manifestly do not remedy the basic inadequacies of the primary references to make obvious the now claimed invention. The Examiner only relies on Kreuter to teach that various polymers are known as equivalents for nanoparticles used for in vivo delivery and on Jans that the specific polysorbate 85 is known in the prior art for use in particle formulation for drug delivery. As such, these references manifestly do not cure the basic deficiencies of the other prior art to make obvious Applicants' discovery.

Accordingly, withdrawal of the rejection of the claims remaining, i.e., Claims 101-122, 132 and 133, limited to the method of making and their allowance is requested.

It is submitted that this application is now in condition for allowance and which is solicited.

Respectfully submitted,

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IN THE CLAIMS

88-100. (Canceled).

123-131. (Canceled).

134. (Canceled).